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| | | | | Application Number | 10/728,521-Conf. #8270 |
| | | | | Filing Date | December 5, 2003 |
| | | | | First Named Inventor | Atul Varadhachary |
| | | | | Art Unit | 1656 |
| | | | | Examiner Name | C. M. Kam |
| Sheet | 1 | of | 4 | Attorney Docket Number | HO-P02703US2 |

| U.S. PATENT DOCUMENTS | | | | | | |
|-----------------------|--------------------------|---|--|--------------------------------|--|---|
| Examiner Initials* | Cite No. ¹ | Document Number | | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| | | Number-Kind Code ² (if known) | | | | |
| /CMK | AA* | US-4,977,137 | | 12-11-1990 | Nichols et al. | |
| | AB* | US-5,198,419 | | 03-30-1993 | Ando et al. | |
| | AC* | US-5,457,093 | | 10-10-1995 | Cini et al. | |
| | AD* | US-5,561,109 | | 10-01-1996 | Mita et al. | |
| | AE* | US-5,571,691 | | 11-05-1996 | Conneely et al. | |
| | AF* | US-5,571,896 | | 11-05-1996 | Conneely et al. | |
| | AG* | US-5,571,697 | | 11-05-1996 | Conneely et al. | |
| | AH* | US-5,576,299 | | 11-19-1996 | Ando et al. | |
| | AI* | US-5,766,939 | | 06-16-1998 | Conneely et al. | |
| | AJ* | US-5,834,424 | | 11-10-1998 | Valenti et al. | |
| | AK* | US-5,849,881 | | 12-15-1998 | Conneely et al. | |
| | AL* | US-5,955,316 | | 09-21-1999 | Conneely et al. | |
| | AM* | US-6,025,326 | | 02-15-2000 | Steinberg, et al. | |
| | AN* | US-6,066,469 | | 05-23-2000 | Kruzel et al. | |
| | AO* | US-6,080,559 | | 06-27-2000 | Conneely et al. | |
| | AP* | US-6,096,731 | | 08-01-2000 | McDonald | |
| | AQ* | US-6,100,054 | | 08-08-2000 | Conneely et al. | |
| | AR* | US-6,111,081 | | 08-29-2000 | Conneely et al. | |
| | AS* | US-6,228,614 | | 05-08-2001 | Conneely et al. | |
| | AT* | US-6,333,311 | | 12-25-2001 | Nuijens et al. | |
| | AU* | US-6,399,570 | | 06-04-2002 | Mann | |
| | AV* | US-6,635,447 | | 10-21-2003 | Conneely et al. | |
| | AW* | US-20020016289 | | 02-07-2002 | Conneely | |
| | AX* | US-2003/0096736-A1 | | 05-22-2003 | Kruzel et al. | |
| | AY* | US-2003/0105006-A1 | | 06-05-2003 | Mann | |
| | AZ* | US-2003/0190303-A1 | | 10-09-2003 | KIMBER et al. | |
| | AA1* | US-2003/0203839-A1 | | 10-30-2003 | Kruzel et al. | |
| | AB1* | US-2004/0009896-A1 | | 01-15-2004 | Glynn et al. | |
| | AC1* | US-2004/0009895-A1 | | 01-15-2004 | Varadhachary et al. | |
| | AD1* | US-2004/0082504-A1 | | 04-29-2004 | Varadhachary et al. | |
| | AE1* | US-2004/0142037-A1 | | 07-22-2004 | Engelmayer et al. | |
| | AF1* | US-2004/0151784-A1 | | 08-05-2004 | Varadhachary et al. | |
| | AG1* | US-2004/0152624-A1 | | 08-05-2004 | Varadhachary et al. | |
| | AH1* | US-2004/0152623-A1 | | 08-05-2004 | Varadhachary et al. | |
| | AI1* | US-2004/0176276-A1 | | 09-09-2004 | Varadhachary et al. | |
| | AJ1* | US-2005/0004006-A1 | | 01-06-2005 | Engelmayer et al. | |
| | AK* | US-2005/0019342-A1 | | 01-27-2005 | Varadhachary et al. | |
| | AL* | US-2005/0064546-A1 | | 03-24-2005 | Conneely et al. | |
| /CMK | AM* | US-2005/0075277-A1 | | 04-07-2005 | Varadhachary et al. | |

| FOREIGN PATENT DOCUMENTS | | | | | | | |
|--------------------------|--------------------------|---|--|-----------------------------------|--|--|----------------|
| Examiner Initials* | Cite No. ¹ | Foreign Patent Document | | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear | T ⁶ |
| | | Country Code ² -Number ⁴ -Kind Code ³ (if known) | | | | | |
| Examiner Signature | | /Chih-Min Kam/ | | | Date Considered | 06/30/2007 | |

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| Sheet | 2 | of | 4 | Attorney Docket Number | HO-P02703US2 |

| | | | | | | |
|-------|----|----------------|------------|------------------------------------|--|--|
| /CMK/ | BA | WO-9221752 | 12-10-1992 | The United States of America | | |
| | BB | EP-0584558 | 03-02-1994 | Snow Brand Milk Prod Co Ltd | | |
| | BC | JP-07233086 | 09-05-1995 | Morinaga Milk Industry Co Ltd | | |
| | BD | EP-0730868 | 09-11-1996 | Tamotsu Satch | | |
| | BE | WO-9833509 | 08-06-1998 | Pharming Intellectual Property Bv | | |
| | BF | WO-0203910-A2 | 01-17-2002 | Yakubovskaya Ralsa Ivanovna et al. | | |
| /CMK/ | BG | WO-02100445-A1 | 12-19-2002 | The University of Sydney | | |

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. * CITE NO.: Those application(s) which are marked with an single asterisk (*) next to the Cite No. are not supplied (under 37 CFR 1.98(a)(2)(iii)) because that application was filed after June 30, 2003 or is available in the IFW. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

| NON PATENT LITERATURE DOCUMENTS | | | | | | |
|---------------------------------|-----------------------|---|--|--|--|----------------|
| Examiner Initials | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | | | | T ² |
| /CMK/ | CA | ARNOLD et al, "Bactericidal Activity of human Lactoferrin: Sensitivity of a Variety of Microorganisms," Infection and Immunity Vol. 28, No. 3, June 1980, pgs 893 - 898. | | | | |
| | CB | ARTYM et al, "Lactoferrin Restoration of Lymphocyte and Macrophage Content in Cyclophosphamide-Treated mice," Cellular & Molecular Biology Letters Vol. 7, Sept. 2002, pg 37. | | | | |
| | CC | ARTYM et al, "Normalization of Peripheral Blood Cell Composition by Lactoferrin in Cyclophosphamide-treated Mice," Med Sci Monit. Vol. 10 No. 3, 2003, pgs BR84-89. | | | | |
| | CD | ARTYM et al, "Orally Administered Lactoferrin Restores Humoral Immune Response in Immunocompromised Mice," Immunology Letter Vol. 89, 2003, pgs. 9 -15. | | | | |
| | CE | ARTYM et al, "Reconstitution of the Cellular Immune Response by Lactoferrin in Cyclophosphamide-treated mice is Correlated with Renewal of T Cell compartment," Immunobiol. Vol. 207, 2003, pgs 197-205. | | | | |
| | CF | BELLAMY et al, "Killing of Candida Albicans by lactoferrin B, a Potent Antimicrobial Peptide derived from the N-terminal Region of Bovine Lactoferrin," Med Microbial Immunol. Vol. 182, 1993, pgs 97 - 105. | | | | |
| | CG | BRINK, "Lactoferrin: The Bioactive Peptide that Fights Disease," Life Extension Magazine, found at http://www.lef.org/LEFCMS/asp/PringVersionMagic.aspx?CmsID=31812 , October, 2000. | | | | |
| | CH | CLARKE et al, "Evaluation of Bovine Lactoferrin as a Topical Therapy for Chemotherapy-Induced Mucositis in the Golden Syrian Hamster," Oral Oncology 35, 1999, pp. 197-202. | | | | |
| | CJ | CUMBERBATCH et al, "IL-1 B-induced Langerhans' cell Migration and TNF-A production in Human Skin: Regulation by Lactoferrin," Clin Exp. Immunol 132, 2003, pp. 352-359. | | | | |
| | CK | CUMBERBATCH et al, "Regulation of Epidermal Langerhans Cell Migration by Lactoferrin," Immunology 2000, 100, pp. 21-28. | | | | |
| | CM | DIAL et al, "Effect of Lactoferrin of Helicobacter felis Induced Gastritis," Biochem. Cell Biol. Vol. 80, 2002, pgs 113 - 117. | | | | |
| | CM1 | DONNELLY, et al., Antimicrobial therapy to prevent or treat oral mucositis. Lancet Infect Dis. 2003 Jul; 3(7):405 | | | | |
| /CMK/ | CN | ELLISON et al, "Damage of the Outer Membrane of Enteric gram-Negative Bacteria by Lactoferrin and Transferrin," Infection and Immunity Vol. 56 No. 11, November 1988, pgs 2774 | | | | |

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|--------------------|----------------|-----------------|------------|
| Examiner Signature | /Chih-Min Kam/ | Date Considered | 06/30/2007 |
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| | | Attorney Docket Number | HO-P02703US2 |
| Sheet | 3 | of | 4 |

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|------|-----|---|--|
| | | - 2781. | |
| /CMK | CO | FUJIHARA et al, "Lactoferrin Protects Against UV-B Irradiation-Induced Corneal Epithelial Damage in Rats," Cornea 19(2); 2000, pp. 207-211. | |
| | CP | HARMSEN et al, "Antiviral Effects of Plasma and Milk Proteins: Lactoferrin Shows Potent Activity against Both Human Immunodeficiency Virus and Human cytomegalovirus Replication in Vitro," Journal of Infectious Diseases Vol. 172, 1995, pgs 380 - 388. | |
| | CQ | HE et al, "The Inhibition of Mast Cell Activation by Neutrophil Lactoferrin: Uptake by Mast Cells and Interaction with Trypsin, Chymase and Cathepsin G," Biochemical Pharmacology 65, 2003, pp. 1007-1015. | |
| | CR | IKEDA et al, "Lactoferrin Markedly Inhibits Hepatitis C Virus Infection in Cultured Human Hepatocytes," Biochemical and Biophysical Research Communications Vol. 245, 1998, pgs 549 - 553. | |
| | CS | INOUE et al, "Colostrum and severe gut GVHD," Bone Marrow transplant Vol 22 No. 4, 1998, pgs 402- 403. | |
| | CT | INOUE et al, "Lactoferrin and Gut GVHD," 5th annual Conference on Lactoferrin, Banff, Canada 2001. | |
| | CU | ISAMIDA et al, "Protective Effect of Lactoferrin against Toxoplasma Gondii Infection in Mice," J Vet Med Sci. Vol. 60 No 2, 1998, pgs 241 - 244. | |
| | CV | KIMBER et al, "Lactoferrin and Regulation of Cutaneous Immunity and inflammation," Elsevier Science B.V., 2000, pgs 87-93. | |
| | CW | KIMBER et al, "Lactoferrin: Influence on Langerhans Cells, Epidermal Cytokines, and Cutaneous Inflammation," Biochem Cell Biol. 80, 2002, pp. 103-107. | |
| | CX | KUHARA, T. et al., (2000) "Orally administered lactoferrin exerts an antimetastatic effect and enhances production of IL-18 in the intestinal epithelium" Nutrition and Cancer, Vol. 28(2), pp. 192-199. | |
| | CY | KUIPERS et al, "Synergistic Fungistatic Effects of Lactoferrin in Combination with Antifungal Drugs against Clinical Candida Isolates," Antimicrobial agents and Chemotherapy Vol. 43, No. 11, November 1999, pgs 2635-2641. | |
| | CZ | LEGRAND et al, "The N-terminal Arg2, Arg3, Arg4 of Human Lactoferrin Interact with Sulphated Molecules but Not with the Receptor Present on Jurkat Human Lymphoblastic T-Cells," Biochem J Vol. 327, pp. 841-846 (1997). | |
| | CA1 | LEVAY et al, "Lactoferrin: A General Review," Haematologica Vol. 80, 1995, pgs 252-267. | |
| | CB1 | MAKKONEN, et al., Granulocyte macrophage; Int. J. Radiation Oncology; Biol. Phys.; 2000; Vol. 46 (3); 525-534. | |
| | CC1 | MARCHETTI et al, "Metal Complexes of Bovine Lactoferrin Inhibit in vitro Replication of Herpes Simplex Virus Type 1 and 2," BioMetals Vol. 11, 1998, pgs 89-94. | |
| | CD1 | MASSON et al, "Lactoferrin in Milk from Different Species," Comp. Biochem. Physiol. Vol. 39B, 1971, pgs 119 -129. | |
| | | MATTHEWS et al, "Antiviral Activity in milk of Possible Clinical Importance," The Lancet, December 1976, pgs 1387 - 1389. | |
| | CE1 | METZ-BOUTIGUE et al., "Human Lactotransferrin: Amino Acid Sequence and Structural Comparisons with other transferrins," Eur J. Biochem. Vol. 145, 1984, pgs 659 - 676. | |
| | CF1 | MIEHLKE et al, "Direct Activity of recombinant Human Lactoferrin against Helicobacter Pylori," Journal of Clinical Microbiology, Oct. 1996, pgs 2593 - 2594. | |
| | CG1 | NAKAJIMA et al, "Lactoferrin as a Suppressor of Cell Migration of Gastrointestinal Cell Lines," Journal of Cellular Physiology 170, 1997, pp. 101-105. | |
| /CMK | CH1 | SATO et al, "Oral Administration of Bovine Lactoferrin for Treatment of Intractable Stomatitis in Feline Immunodeficiency Virus (FIV)-positive and FIV-negative Cats," AJVR Vol. 57 No. 10, | |

| | | | |
|--------------------|----------------|-----------------|------------|
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|--------------------|----------------|-----------------|------------|

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| | | | |
|-------|-----|--|--|
| | | October 1996, pgs 1443 - 1446. | |
| /CMK/ | CI1 | SHIH, et al., A Research Review of the Current Treatments for Radiation, Oncology Nursing Forum; August 2002, Vol. 29 (7); 1063-1080. | |
| | CJ1 | TAKAKURA et al, "Effect of Orally Administered Bovine Lactoferrin on the immune Response in the Oral Candidiasis Murine Model," J Med Microbiol Vol 53, Pt. 6, Jun 2004, pgs 495-500. | |
| | CK1 | TAKAKURA et al, "Oral Lactoferrin Treatment of Experimental Oral Candidiasis in Mice," Antimicrobial Agents and Chemotherapy Vol. 47 No. 8, August 2003, pgs. 2619-2623. | |
| | CL1 | TAKAYAMA et al, "Effects of Lactoferrin on Collagen Gel Contractile Activity and Myosin Light Chain Phosphorylation in Human Fibroblasts," FEBS Letter 508, 2001, pp. 111-116. | |
| | CL2 | TAKAYAMA et al, "The Bovine Lactoferrin Region Responsible for Promoting the Collagen Gel Contractile activity of Human Fibroblasts," Biochemical and Biophysical Research Communications 299 (2002), pp 813-817. | |
| | CM1 | TOMITA et al, "Potent Antibacterial Peptides Generated by Pepsin Digestion of Bovine Lactoferrin," J Dairy Sci Vol. 74, 1991, pgs 4137 - 4142. | |
| | CN1 | TRUMPLER et al, "Antibacterial Prophylaxis with Lactoferrin in Neutropenic Patients," Eur. J. Clin. Microbiol. Infect. Dis. Vol. 8, no. 4, 1989, pgs 310 - 313. | |
| | CO1 | VAN BERKEL et al, "N-terminal Stretch Arg2, Arg3, and Arg5 of Human Lactoferrin is Essential for Binding to Heparin, Bacterial Lipopolysaccharide, Human Lysozyme and DNA," Biochem J. Vol. 328, pp. 145-151 (1997). | |
| | CP1 | VORLAND et al, "Lactoferrin: A Multifunctional Glycoprotein," APMIS Vol. 107, 1999, pgs. 971-981. | |
| | CQ1 | WARD et al, "A System for Production of Commercial Quantities of Human Lactoferrin: A Broad Spectrum Natural Antibiotic," Biotechnology Vol. 13, may 1995, pgs 498 - 503. | |
| | CR1 | WARD et al, "Lactoferrin and Host Defense," Biochem Cell Biol. 80, 2002, pp. 95-102. | |
| | CS1 | WEINBERG, Eugene, "The Therapeutic Potential of Lactoferrin," Expert Opinion Investig. Drugs, 12(5), 2003, pp. 841-851. | |
| | CT1 | YAMAGUCHI et al, "Potential Usefulness of Bovine Lactoferrin for Adjunctive Immunotherapy for Mucosal Candida Infections," Biometals Vol. 17 No. 3, June 2004, pgs 245 - 248. | |
| | CU1 | YANG et al, "Antitumor Activity and Specificity as a Function of Substitutions in the Lipophilic Sector of Helical Lactoferrin-derived Peptide," Journal of Peptide Science 9, 2003, pp. 300-311. | |
| /CMK/ | CV1 | YANG et al., "Enhanced Antitumor Activity and Selectivity of Lactoferrin-derived peptides," J. Peptide Res. 60, 2002, pp. 187-197. | |

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